CONFIDENTIAL
ATTY. WORK PRODUCT

REC 001995
AU Benowitz,N
TTL Clinical Pharmacology of Nicotine
CT Annu Rev Med 37: 21
DT 1986
SUM **Nicotine is not effective in reducing smoking in smokers who are not trying to quit.** Nicotine gum has been shown to be useful in smoking cessation treatment in several, but not all, trials. The gum is most effective when used as part of a comprehensive program such as in smoking cessation clinics. Typical results from such trials are 30-40% one-year abstinence compared to 15-20% for placebo-treated patients. **Use of nicotine gum in general medical practice is less encouraging.** Two large studies have been reported. In one (not placebo controlled), one-year abstinence was 9% for nicotine gum vs 4% for physician advice or no intervention. In the other, the British Thoracic Society study of verbal advice combined with nicotine or placebo gum, there was no difference in outcome (10% one-year abstinence for all treatments).
SUBJ K1ABA, CESSATION, METHODS, PHARMACOLOGICAL, NICOTINE REPLACEMENT
CD APRIL 2, 1987 JD/WC
UDT MAY 1, 1987 SHB

REC 002771
AU Benowitz,N; Jones,R; Jacob,P
TTL Additive Cardiovascular Effects of Nicotine and Ethanol
CT Clin Pharmacol Ther 40(4): 420-424
DT 1986
SUM
SUBJ
CD NOVEMBER 1, 1987 SHB

2024987944

Source: https://www.industrydocuments.ucsf.edu/docs/nnvb0003

REC 001548
AU Benowitz,NL
TTL
CT The Use Of Biologic Fluid Samples In Assessing Tobacco Smoke Consumption
DT
SUM In summary, the use of thiocyanate levels as a marker of smoke consumption has fairly good specificity and sensitivity in studying active smokers, has the advantage of a long half-life such that the time of sampling is not critical, and is inexpensive to measure. The limitations are that specificity and sensitivity may be inadequate in light smokers or in smokers who have cut down on their smoking. In addition, the long half-life of thiocyanate makes it impossible to use it to assess recent smoking behavior. Due to other sources or cyanide, thiocyanate is not a good quantitative indicator of consumption of tobacco smoke.; The limitation in using carbon monoxide as a measurement of tobacco smoke consumption per se are that the time of day and the length of time since smoking the last cigarette influence carbon monoxide levels and that there is considerable individual variation in carbon monoxide absorption and elimination characteristics, depending on smoking habits, disease state, and activity level.; In this paper, I will focus on the use of carbon monoxide, thiocyanate, nicotine, and cotinine as markers of smoke consumption. Factors influencing absorption of these substances from smoke, elimination from the body, kinetic characteristics that relate to their usefulness as markers of smoke exposure, and limitations of their use are discussed. Before discussing the individual compounds, it should be emphasized that 1) The relative intake of different pharmacologically active substances differs among different tobacco products and different smokers and 2) Intake cannot be equated with exposure. With respect to the latter, both rate of intake (dose) and rate of elimination determine the average exposure level.; In the smoker who is a light smoker of who has cut down during smoking cessation treatment, the thiocyanate level approaches levels due to dietary sources of cyanide, making documentation on smoking status increasingly more difficult.; Blood concentration of nicotine can be measured by gas chromatography (Jacob et al. 1981), radioimmunoassay (Langone et al. 1973), and possibly high performance liquid chromatography. Sample preparation is problematic in that contamination of samples with even small amount of tobacco smoke can substantially elevate the normally low concentrations of nicotine in the blood. Thus, careful precautions against contamination during both sample collection and processing for analysis are essential. Because the concentrations are so low, measurement of nicotine in the blood has been difficult for many laboratories in the past, but with currently available assays, it is feasible for large scale epidemiologic studies. Measurement of urinary levels of nicotine has been suggested as a marker for qualitatively useful, but quantitatively it is limited by the fact that there is variation in renal elimination of nicotine depending on urine pH and flow rate so that it is difficult to extrapolate from urine to blood concentrations of nicotine.
SUBJ R1, PHARMACOKINETICS
CD APRIL 2, 1987 JD/WC

2024987945

Source: https://www.industrydocuments.ucsf.edu/docs/nnvb0003

UDT MAY 1, 1987 SHB

REC 001143
AU Benowitz,NL; Kuyt,F; Peyton,J
TTL Circadian Blood Nicotine Concentrations During Cigarette Smoking
CT Clin Pharmacol 32: 758-764
DT 1982
SUM Although evidence of regulation appears convincing, the methods of assessing nicotine consumption and levels of nicotine in the body have been indirect, being based on number of cigarettes smoked or puffing characteristics, consumption of other smoke constituents such as carbon monoxide, or occasional blood nicotine or cotinine or urinary nicotine or cotinine levels. Occasional blood nicotine concentrations are difficult to interpret because of the relatively short distribution half-life (t 1/2) and the substantial influence of nicotine delivered from the preceding cigarette. Urinary nicotine levels do not precisely reflect blood nicotine concentrations because urinary excretion is dependent on urinary pH and urine flow rate. Blood and urinary cotinine reflect nicotine intake but, because of differences in fractional conversion of nicotine to cotinine or differences in rate of metabolism of cotinine among individuals, may be an imperfect reflection of nicotine concentrations. To better characterize daily exposure to nicotine, we studied hospitalized volunteer smokers by means of a Circadian blood-sampling method. We studied nicotine levels while subjects smoked their usual brands or low- or high-nicotine research cigarettes. We found wide interindividual variation in nicotine levels even when these level were normalized on the basis of machine-predicted nicotine delivery. We also found evidence of nicotine regulation when comparing high-nicotine with subjects' own cigarettes, but no nicotine regulation with low-nicotine cigarettes.
SUBJ E1BA, MOTIVATIONS, MAINTENANCE, TITRATION
CD APRIL 2, 1987 JD/WC
UDT MAY 1, 1987 SHB

2024987946

Source: https://www.industrydocuments.ucsf.edu/docs/nnvb0003

REC 001144
AU Benowitz,NL; Kuyt,F; Peyton,J
TTL Circadian Blood Nicotine Concentrations During Cigarette Smoking
CT Clin Pharmacol 32: 758-764
DT 1982
SUM Although evidence of regulation appears convincing, the methods of assessing nicotine consumption and levels of nicotine in the body have been indirect, being based on number of cigarettes smoked or puffing characteristics, consumption of other smoke constituents such as carbon monoxide, or occasional blood nicotine or cotinine or urinary nicotine or cotinine levels. Occasional blood nicotine concentrations are difficult to interpret because of the relatively short distribution half-life (t 1/2) and the substantial influence of nicotine delivered from the preceding cigarette. Urinary nicotine levels do not precisely reflect blood nicotine concentrations because urinary excretion is dependent on urinary pH and urine flow rate. Blood and urinary cotinine reflect nicotine intake but, because of differences in fractional conversion of nicotine to cotinine or differences in rate of metabolism of cotinine among individuals, may be an imperfect reflection of nicotine concentrations. To better characterize daily exposure to nicotine, we studied hospitalized volunteer smokers by means of a Circadian blood-sampling method. We studied nicotine levels while subjects smoked their usual brands or low- or high-nicotine research cigarettes. We found wide interindividual variation in nicotine levels even when these level were normalized on the basis of machine-predicted nicotine delivery. We also found evidence of nicotine regulation when comparing high-nicotine with subjects' own cigarettes, but no nicotine regulation with low-nicotine cigarettes.
SUBJ R1A, PHARMACOKINETICS, NICOTINE
CD APRIL 2, 1987 JD/WC
UDT MAY 1, 1987 SHB

REC 001384
AU Benowitz,NL; Peyton,J III; Jones,RT; Rosenberg,J
TTL Interindividual Variability in the Metabolism and Cardiovascular Effects of Nicotine in Man
CT J Pharmarcol Exp Ther 221: 368-372
DT 1982
SUM Cigarette smoking and nicotine ingestion are known to constrict cutaneous blood vessels and decrease blood flow to hands and feet (Roth et al., 1944; Eckstein et al., 1957). Skin temperature is related to cutaneous blood flow. Fingertip and toe temperatures consistently fall after nicotine exposure. We found that, in contrast to the heart rate response, the reduction in skin temperature was progressive during nicotine infusion. The magnitude of the response was directly related to the blood concentration of nicotine during and after nicotine infusion. There was no evidence of tolerance.
SUBJ J1A, TOLERANCE, NICOTINE
CD APRIL 2, 1987 JD/WC
UDT MAY 1, 1987 SHB

2024987947

Source: https://www.industrydocuments.ucsf.edu/docs/nnvb0003

REC 001385
AU Benowitz,NL; Peyton,J III; Jones,RT; Rosenberg,J
TTL Interindividual Variability in the Metabolism and Cardiovascular Effects of Nicotine in Man
CT J Pharmarcol Exp Ther 221: 368-372
DT 1982
SUM Cigarette smoking accelerates the metabolism of many drugs including nicotine (Jusko, 1978; Beckett et al., 1971). The degree of acceleration cannot be predicted from the number of cigarettes reported smoked. Plasma cotinine, the major metabolite of nicotine, is potentially a marker of nicotine consumption (Gorrod and Jenner, 1975; Langone et al., 1973). It might be hypothesized that cotinine would be a better indicator of tobacco smoke exposure and effects on drug metabolism. However, we found no relationship between cotinine concentration and metabolic clearance of nicotine. In studies with rodents, nicotine metabolic clearance appears dose-dependent (Miller et al., 1977). However, our data in humans give no evidence of dose dependence.
SUBJ R1A, PHARMACOKINETICS, NICOTINE
CD APRIL 2, 1987 JD/WC
UDT MAY 1, 1987 SHB

REC 000687
AU Benowitz,NL; Jacob,P
TTL Daily Intake Of Nicotine During Cigarette Smoking
CT Clin Pharmacol Ther 35(4): 499-504
DT 1984
SUM The importance of nicotine in the maintenance of cigarette smoking behavior and its contribution to adverse effects of smoking are generally accepted, but no adequate methods for determining daily nicotine intake have been described. Nicotine intake from single cigarettes has been measured by spiking cigarettes with radiolabeled nicotine, but is not applicable in the determination of nicotine consumption in natural smoking situations. Blood concentrations of nicotine sampled throughout the day are useful in estimating nicotine exposure, but translation of blood concentrations into intake is theoretically limited by the fact that metabolic clearance varies considerably from person to person. Thus a given blood concentration of nicotine may represent dose levels of nicotine that differ severalfold for different people.
SUBJ V1, RESEARCH CRITICISM
CD APRIL 2, 1987 JD/WC
UDT MAY 1, 1987 SHB

2024987948

Source: https://www.industrydocuments.ucsf.edu/docs/nnvb0003

REC 001235
AU Benowitz,NL; Peyton,J
TTL Nicotine and Carbon Monoxide Intake from High- and Low-yield Cigarettes
CT Clin Pharmacol Ther 36(2): 265-270
DT 1984
SUM We found that our subjects maintained the same blood level of nicotine and carbon monoxide while they were smoking popular high- and low-yield commercial cigarettes, despite the fact that the low-yield cigarettes were rated as being of much poorer quality than the usual brand cigarettes. Consumption of desired nicotine dose was accomplished primarily by obtaining 60% more nicotine per low-yield cigarette than the yield predicted by FTC smoking machine assays. High-yield cigarettes were smoked less efficiently; intake was 76% of that predicted. Also, more (25%) of the low-yield cigarettes were smoked a day. It is noteworthy that although more low-yield cigarettes were smoked a day, the same total weight of tobacco of all brands was smoked. As we have reported, there is no difference in percent nicotine per gram tobacco in these brands, so it is not surprising that smoking the same weight of tobacco results in the same nicotine delivery. Subjects' higher nicotine levels while smoking the usual brand of cigarettes may relate in part to the pleasure of smoking a cigarette with which one is familiar and enjoys and in part to maintaining a particular nicotine blood level. Other brands were judged not as pleasurable and were smoked in such a way that the nicotine blood level was about 70% of that while smoking their usual brand cigarettes. The findings that nicotine intake while smoking the usual brand of cigarettes correlated strongly with that from high- or low-yield brands within subjects and that intake levels were the same for high- and low-yield cigarettes suggest that each individual has his or her own acceptable lower limit for nicotine. We speculate that intake below this level might be associated with manifestations of nicotine abstinence.; We studied only one brand of low-yield cigarettes that was in the 5-mg tar class. There is recent evidence that the smoking of ultralow-yield cigarettes in the 1-mg tar class results in reduced nicotine intake, although much less than that predicted by the FTC.
SUBJ E1BA, MOTIVATIONS, MAINTENANCE, TITRATION
CD APRIL 2, 1987 JD/WC
UDT MAY 1, 1987 SHB

2024987949

Source: https://www.industrydocuments.ucsf.edu/docs/nnvb0003

REC 001382
AU Benowitz,NL; Kuyt,F; Jacob,P
TTL Influence of Nicotine on Cardiovascular and Hormonal Effects of Cigarette Smoking
CT Clin Pharmacol Ther 3691
DT July, 1984
SUM As reported by many, cigarette smoking increased hr; this increase averaged 7.4 bpm over 24 hr. Hr increased more after the first few cigarettes of the day in all smoking conditions than when abstaining, and then followed a circadian pattern similar to that in the abstention period or in nonsmokers. Not only was hr higher during smoking days, it was also higher overnight after smoking days than after nonsmoking days, even through no cigarettes were smoked after 11 p.m. Despite markedly different blood nicotine concentrations, hr did not differ when smoking ln or hn or usual brand cigarettes. This contrasts with reports of higher hrs after smoking one or several hn cigarettes than after ln cigarettes.
SUBJ F1A, PHYSIOLOGICAL EFFECTS, NICOTINE
CD APRIL 2, 1987 JD/WC
UDT MAY 1, 1987 SHB

2024987950

Source: https://www.industrydocuments.ucsf.edu/docs/nnvb0003

REC 001253
AU Benowitz,NL; Jacob,P III
TTL Nicotine Renal Excretion Rate Influences Nicotine Intake During Cigarette Smoking
CT J Pharmacol Exp Ther 234(1): 153
DT 1985
SUM Daily nicotine intake was 18% greater during the acid compared with the alkali loading condition. On average, smokers consumed more nicotine per cigarette during acid compared with alkali loading but not when compared with base line or placebo.; Acidification increased urinary nicotine clearance by 200%. Alkalinization decreased clearance by 78% of placebo treatment values. Total clearance (renal plus metabolic) increased 41% and decreased 1%, respectively. On average, half the increased urinary excretion was compensated for by increased nicotine intake. Compensation was incomplete based on the observation that average nicotine blood levels declined by 15% in the acid loading condition. On an average, smokers smoked the same number of cigarettes in acid and alkaline conditions, indicating that differences in nicotine intake were achieved by changes in smoking behavior, perhaps alterations in puff and inhalation volumes or number (Herning et al., 1983). Carbon monoxide levels were not useful as an indicator of nicotine intake in this study. Caution should be exercised in applying the findings to usual smoking situations. We performed our studies under conditions of extreme urinary acidification or alkalinization, so that the changes in renal clearance would be maximized. Even with extreme differences in urinary pH, differences in overall nicotine elimination rate and smoking behavior were modest. This is because renal excretion is a minor pathway for elimination of nicotine; most is metabolized. Smaller changes in urinary pH, such as occur spontaneously throughout the day or that might be related to stressful events, would not be expected to substantially influence nicotine elimination or smoking behavior.
SUBJ E1BA, MOTIVATIONS, MAINTENANCE, TITRATION
CD APRIL 2, 1987 JD/WC
UDT MAY 1, 1987 SHB

REC 003086
AU Benowitz,NL
TTL Clinical Pharmacology of Nicotine Gum
CT The Pharmacologic Treatment of Tobacco Dependence: Proceedings of the World Congress, November 4-5, 1985 (Smoking Behavior and Policy Conference Series) pp. 108-119
DT 1986
SUM . . . analysis of the relationship between cardiovascular effects and nicotine levels over time using hysteresis plots suggests substantial but incomplete development of tolerance to heart rate acceleration, no tolerance to skin temperature changes, and partial tolerance to blood pressure elevation. (p. 115)
SUBJ J1A, TOLERANCE, NICOTINE
CD JANUARY 1, 1988 SHB

2024987951

Source: https://www.industrydocuments.ucsf.edu/docs/nnvb0003

REC 003087
AU Benowitz,NL
TTL Clinical Pharmacology of Nicotine Gum
CT The Pharmacologic Treatment of Tobacco Dependence: Proceedings of the World Congress, November 4-5, 1985 (Smoking Behavior and Policy Conference Series) pp. 108-119
DT 1986
SUM From these studies we have determined that after its initial decline (i.e., nicotine moving from blood into tissues) the half-life (the time it takes for nicotine level to fall by one-half), is about two hours. (p. 108); Thus, nicotine will accumulate in the body of a regular user over the day. It also means that if there is a significant level of nicotine at bedtime, significant levels (p. 108) of nicotine (about 5% or 10% of the level of the night before) will be present even at waking in the morning after several hours of abstinence. (p. 110)
SUBJ R1A, PHARMACOKINETICS, NICOTINE
CD JANUARY 1, 1988 SHB

REC 002846
AU Benowitz,NL; Jacob,P III; Savanapridi,C
TTL Determinants of Nicotine Intake While Chewing Nicotine Polacrilex Gum
CT Clin Pharmacol Ther 41(4): 467-473
DT 1987
SUM However, the success rate with nicotine gum is still disappointingly low, adding only 5% to 20% abstinence compared with placebo or no gum conditions. (p. 467)
SUBJ E1H, MOTIVATIONS, NICOTINE GUM
CD NOVEMBER 1, 1987 SHB

REC 002722
AU Benowitz,NL; Jacob,P; Savanapridi,C
TTL Determinants of nicotine intake while chewing nicotine polacrilex gum
CT Clin Pharmacol Ther 41: 467-473
DT April, 1987
SUM . . . the success rate with nicotine gum is still disappointingly low, adding only 5% to 20% abstinence compared with placebo or no gum conditions. (p. 467)
SUBJ K1ABA, CESSATION, METHODS, PHARMACOLOGICAL, NICOTINE REPLACEMENT
CD OCTOBER 1, 1987 SHB
CHAR MF

REC 003249
AU Benowitz,NL; Lake,t; Keller,KH; Lee,BL
TTL Prolonged Absorption with Development of Tolerance to Toxic Effects after Cutaneous Exposure to Nicotine
CT Clin Pharmacol Ther 42(1): 119-120
DT July, 1987
SUM
SUBJ
CD FEBRUARY 1, 1988 SHB

2024987952

Source: https://www.industrydocuments.ucsf.edu/docs/nnvb0003

REC 002877
AU Gori,GB; Benowitz,NL; Lynch,CJ
TTL Mouth Versus Deep Airways Absorption of Nicotine in Cigarette Smokers
CT Pharmacol Biochem Behav 25: 1181-1184
DT 1986
SUM
SUBJ
CD NOVEMBER 1, 1987 SHB

REC 002163
AU Hall,SM; Herning,RI; Jones,RT; Benowitz,NL; Jacob,P
TTL Blood Cotinine Levels As Indicators of Smoking Treatment Outcome
CT Clin Pharmacol Ther 35(6): 810-814
DT 1984
SUM All dropouts were asked why they left the treatment program. All gave primarily psychologic or situational reasons (eg, a dislike of group participation or other stressful events that made it impossible to quit smoking). None mentioned withdrawal symptoms, craving, or any factor that at face value would implicate tobacco dependence.
SUBJ I1A, WITHDRAWAL, NICOTINE
CD APRIL 11, 1987 LSI
UDT JUNE 1, 1987 SHB

REC 002164
AU Hall,SM; Herning,RI; Jones,RT; Benowitz,NL; Jacob,P
TTL Blood Cotinine Levels As Indicators of Smoking Treatment Outcome
CT Clin Pharmacol Ther 35(6): 810-814
DT 1984
SUM All dropouts were asked why they left the treatment program. All gave primarily psychologic or situational reasons (eg, a dislike of group participation or other stressful events that made it impossible to quit smoking). None mentioned withdrawal symptoms, craving, or any factor that at face value would implicate tobacco dependence.
SUBJ K1DA, CESSATION, RELAPSE, NICOTINE
CD APRIL 11, 1987 LSI
UDT JUNE 1, 1987 SHB

2024987953

Source: https://www.industrydocuments.ucsf.edu/docs/nnvb0003

REC 001240
AU Hall,SM; Tunstall,C; Rugg,D; Jones,RT; Benowitz,N
TTL Nicotine Gum and Behavioral Treatment in Smoking Cessation
CT J Consult Clin Psychol 53(2): 256-258
DT 1985
SUM Considerable relapse was noted at 1 year in the gum treatment conditions after gum was no longer available. These data suggest nicotine gum may have to be available to some smokers for longer time periods to prevent delayed relapse. Nicotine gum may be a promising treatment for very dependent smokers. In the present study, cotinine was the best measure of such dependence. It would be useful to develop a more easily obtainable index.
SUBJ K1ABA, CESSATION, METHODS, PHARMACOLOGICAL, NICOTINE REPLACEMENT
CD APRIL 2, 1987 JD/WC
UDT MAY 1, 1987 SHB

REC 001241
AU Hall,SM; Tunstall,C; Rugg,D; Jones,RT; Benowitz,N
TTL Nicotine Gum and Behavioral Treatment in Smoking Cessation
CT J Consult Clin Psychol 53(2): 256-258
DT 1985
SUM Considerable relapse was noted at 1 year in the gum treatment conditions after gum was no longer available. These data suggest nicotine gum may have to be available to some smokers for longer time periods to prevent delayed relapse. Nicotine gum may be a promising treatment for very dependent smokers. In the present study, cotinine was the best measure of such dependence. It would be useful to develop a more easily obtainable index.
SUBJ K1DA, CESSATION, RELAPSE, NICOTINE
CD APRIL 2, 1987 JD/WC
UDT MAY 1, 1987 SHB

REC 001242
AU Hall,SM; Tunstall,C; Rugg,D; Jones,RT; Benowitz,N
TTL Nicotine Gum and Behavioral Treatment in Smoking Cessation
CT J Consult Clin Psychol 53(2): 256-258
DT 1985
SUM Considerable relapse was noted at 1 year in the gum treatment conditions after gum was no longer available. These data suggest nicotine gum may have to be available to some smokers for longer time periods to prevent delayed relapse. Nicotine gum may be a promising treatment for very dependent smokers. In the present study, cotinine was the best measure of such dependence. It would be useful to develop a more easily obtainable index.
SUBJ L1A, QUANTIFICATION, DETERMINANTS
CD APRIL 2, 1987 JD/WC
UDT MAY 1, 1987 SHB

2024987954

Source: https://www.industrydocuments.ucsf.edu/docs/nnvb0003

REC 001243
AU Hall,SM; Tunstall,C; Rugg,D; Jones,RT; Benowitz,N
TTL Nicotine Gum and Behavioral Treatment in Smoking Cessation
CT J Consult Clin Psychol 53(2): 256-258
DT 1985
SUM The use of nicotine gum to treat tobacco dependence assumes (A) smokers smoke in part to obtain nicotine and (B) nicotine absorbed from chewing gum produces pharmacologic effects smokers seek. Clinical trials suggest nicotine gum is more effective than a placebo. Combining the gum with individualized psychosocial treatments has produced 6-month abstinence rates of 63% (Fagerstrom, 1982). If both behavioral and pharmacologic factors are involved in smoking, a treatment that combines behavioral and pharmacologic modalities should be useful. We compared such a treatment with a behavioral treatment alone and with nicotine gum in a low-contact group. Smokers highly dependent on nicotine may be especially good candidates for nicotine gum treatment (Fagerstrom, 1982). In the present study, blood cotinine levels obtained after 8-12 hr of abstinence were used as the primary indicator of nicotine dependence. Cotinine is a nicotine metabolite that has been found to predict smoking treatment outcome (Hall, Herning, Jones, Benowitz, & Jacob, 1984). Number of cigarettes smoked per day at pretreatment and scores on an 8-item scale measuring physical dependence were also used as indicators of nicotine dependence (Fagerstrom, 1982). They were included because they are less expensive and easier to obtain than is cotinine. We hypothesized that (A) the combined treatment condition would produce higher abstinence rates than would either the low-contact nicotine gum treatment or the behavioral treatment alone and that (B) nicotine gum would be more effective for subjects highly dependent on nicotine than for those who were less dependent.
SUBJ K1ABA, CESSATION, METHODS, PHARMACOLOGICAL, NICOTINE REPLACEMENT
CD APRIL 2, 1987 JD/WC
UDT MAY 1, 1987 SHB

2024987955

Source: https://www.industrydocuments.ucsf.edu/docs/nnvb0003

REC 001244
AU Hall,SM; Tunstall,C; Rugg,D; Jones,RT; Benowitz,N
TTL Nicotine Gum and Behavioral Treatment in Smoking Cessation
CT J Consult Clin Psychol 53(2): 256-258
DT 1985
SUM The use of nicotine gum to treat tobacco dependence assumes (A) smokers smoke in part to obtain nicotine and (B) nicotine absorbed from chewing gum produces pharmacologic effects smokers seek. Clinical trials suggest nicotine gum is more effective than a placebo. Combining the gum with individualized psychosocial treatments has produced 6-month abstinence rates of 63% (Fagerstrom, 1982). If both behavioral and pharmacologic factors are involved in smoking, a treatment that combines behavioral and pharmacologic modalities should be useful. We compared such a treatment with a behavioral treatment alone and with nicotine gum in a low-contact group. Smokers highly dependent on nicotine may be especially good candidates for nicotine gum treatment (Fagerstrom, 1982). In the present study, blood cotinine levels obtained after 8-12 hr of abstinence were used as the primary indicator of nicotine dependence. Cotinine is a nicotine metabolite that has been found to predict smoking treatment outcome (Hall, Herning, Jones, Benowitz, & Jacob, 1984). Number of cigarettes smoked per day at pretreatment and scores on an 8-item scale measuring physical dependence were also used as indicators of nicotine dependence (Fagerstrom, 1982). They were included because they are less expensive and easier to obtain than is cotinine. We hypothesized that (A) the combined treatment condition would produce higher abstinence rates than would either the low-contact nicotine gum treatment or the behavioral treatment alone and that (B) nicotine gum would be more effective for subjects highly dependent on nicotine than for those who were less dependent.
SUBJ L1, QUANTIFICATION
CD APRIL 2, 1987 JD/WC
UDT MAY 1, 1987 SHB

REC 002816
AU Hall,SM; Tunstall,C; Rugg,D; Jones,RT; Benowitz,N
TTL Nicotine Gum and Behavioral Treatment in Smoking Cessation
CT J Consul Clin Psychol 53(2): 256-258
DT 1985
SUM **Nicotine gum alone is not a panacea. Promising outcomes have not been reported when minimal psychological support is given with the gum. . . .** (p. 257)
SUBJ K1ABA, CESSATION, METHODS, PHARMACOLOGICAL, NICOTINE REPLACEMENT
CD NOVEMBER 1, 1987 SHB

2024987956

Source: https://www.industrydocuments.ucsf.edu/docs/nnvb0003

REC 001364
AU Herning,RI; Jones,RT; Benowitz,NL; Mines,AH
TTL How a Cigarette is Smoked Determines Blood Nicotine Levels
CT Clin Pharmacol Ther 33(1): 84
DT 1982
SUM It is difficult to examine the pharmacology of tobacco if dose is not well controlled or measured. The dose of nicotine and combustion products a smoker receives from a cigarette is thought to depend partially on machine-determined estimates of the cigarette as well as on smoking technique. The evidence is mostly indirect. The precise relationships between variations in smoking technique, with a full range of smoking behavior measured along with resulting nicotine blood levels, have not been established. Characterizing the relationship between smoking behavior and subsequent drug blood level is important in understanding the regulation mechanisms of smoked delivery of various drugs (i.e., nicotine, tetrahydrocannabinol, cocaine, and opiates). The size of the cigarettes, ventilation characteristics, nicotine and tar ratios, and nicotine content influence the way a person smokes the cigarette and, thus, presumably the dose of nicotine obtained from the cigarette. Setting, duration of tobacco deprivation, stress, urinary pH, and nicotine blood levels also affect the smoker's puffing pattern or number of cigarettes smoked. Thus, how a cigarette is smoked could be as important as, if not more important than, the machine-delivered dose in determining nicotine blood level. Nicotine blood levels after smoking at best correlate only modestly with the machine-delivered dose of the cigarette. Although the accuracy and validity of smoking machine estimates of nicotine and tar delivery are subject to systematic error, a considerable portion of the variability in blood nicotine level may be attributed to individual differences in puffing and inhaling patterns. These aspects of smoking behavior were only partially monitored in earlier studies. For example, we reported that smokers increase puffing when they smoke cigarettes with a lower machine-delivered dose than that of their usual brand, but in that experiment nicotine blood levels were not determined and we did not measure inhalation. While the amounts of smoke drawn into the mouth (puff volume) and into the lungs (inhaled volume) are more difficult to determine than duration or number of puffs, volume measurements are essential to fully characterize relationships between cigarette smoking and blood nicotine levels. Our data suggest that precise measures of exposure to nicotine and probably other smoked drugs are possible in man. The range and relative utility of some measures necessary to adequately measure smoking behavior are illustrated.; Cigarette machine-delivered nicotine yield was the best single measure for predicting blood nicotine increase after smoking. The next best predictors were breath co (fig. 1, b) and number of puffs. Although the correlations of these three measures with blood nicotine levels were statistically significant, the best of the single measures left 73% of the variance unaccounted for.
SUBJ R1A, PHARMACOKINETICS, NICOTINE
CD APRIL 2, 1987 JD/WC
UDT MAY 1, 1987 SHB

2024987957

Source: https://www.industrydocuments.ucsf.edu/docs/nnvb0003

REC 000044
AU Jones,RT; Benowitz,NL; Herning,RI
TTL Clinical Relevance of Cannabis Tolerance and Dependence
CT J Clin Pharmacol 21: 143S-152S
DT 1981
SUM . . . Dependence refers to the appearance of fairly predictable signs and symptoms when drug administration is stopped. The symptoms are decreased or disappear when the drug is restarted or when a pharmacologically similar drug is readministered. Dependence, as used here, does not imply addiction, increased drug seeking or related behavior that may have some relationship to dependence. Such behavior is also determined by environment and personality and genetic, social, and mostly unknown factors. (p. 143S)
SUBJ A1B, TERMS, DEPENDENCE
CD MARCH 1, 1987 SHB

REC 000220
AU Jones,RT; Benowitz,NL; Herning,RI
TTL Clinical Relevance of Cannabis Tolerance and Dependence
CT J Clin Pharmacol 21: 143S-152S
DT 1981
SUM . . . Virtually every psychoactive drug, if given at a dose and a dose schedule producing sustained tissue levels, after a period of time produces measurable tolerance on some indices of drug effects if tested with sensitive, reliable, and appropriate measures at the right time. . . . (p. 143S)
SUBJ J1, TOLERANCE
CD MARCH 1, 1987 SHB

REC 002875
AU Lee,BL; Benowitz,NL; Jacob,P III
TTL Influence of Tobacco Abstinence on the Disposition Kinetics and Effects of Nicotine
CT Clin Pharmacol Ther 41(4): 474-479
DT 1987
SUM
SUBJ
CD NOVEMBER 1, 1987 SHB

Source: https://www.industrydocuments.ucsf.edu/docs/nnvb0003

REC 001289
AU Sachs,DPL; Benowitz,NL; Hall,SM
TTL Paradoxical Cardiovascular Effects of Nicotine During Rapid Smoking Therapy
CT
DT
SUM We conclude, therefore, that there is not a simple, positive relationship between se nic, or nic consumption, and cardiovascular change. Other factors, such as increased vagaltone, saturation of nicotine receptor sites, and changing catecholamine output, could intervene to produce a more complex set of inter-relationships. Importantly, even for patients with COPD or CHD, consuming relatively large amounts of nic, as part of a smoking cessation program, may produce no more cardiovascular stress than small amounts.
SUBJ F1A, PHYSIOLOGICAL EFFECTS, NICOTINE
CD APRIL 2, 1987 JD/WC
UDT MAY 1, 1987 SHB

2024987959

Source: https://www.industrydocuments.ucsf.edu/docs/nnvb0003

REC 001378
AU Schulz,LO; Grunberg,NE; Jonas,S; Benowitz,NL; Hofstetter,A; Schutz,Y; Jequier,E; Wahren,J
TTL
CT Increased 24 Hour Energy Expenditure In Cigarette Smokers
Correspondence
DT
SUM On the basis of the smoking-induced rise in energy expenditure observed in this study, the authors predict that subjects who stop smoking 24 cigarettes per day may be expected to gain as much as 10 kg. The perceived inevitability of weight gain is already used by smokers as a reason for not quitting, and therefore an estimate of this magnitude could have important consequences for public health. Further scrutiny of the "up to 10 kg" prediction (assuming caloric intake does not change) points to factors not given adequate consideration. Whereas a strong argument can be made to support using the subjects as their own controls, the results cannot necessarily be extrapolated to persons who quit smoking. The tacit assumption is that the metabolic difference between a smoker who is smoking and one not allowed to smoke for 24 hours is comparable to the difference between a current smoker and a smoker who has quit. This supposition negates possible adaptive mechanisms in the adjustment of metabolic rate upon withdrawal from nicotine addiction. Adaptive mechanisms in energy expenditure have been shown to occur in response to physical perturbations, such as reduced or increased caloric intake, in a manner that resists changes in body weight. A similar buffering action is feasible in response to nicotine withdrawal. In addition, accumulating evidence points to variations in energy requirements and the efficiency with which food energy is metabolized as a result of genetic differences in metabolic makeup. Although food intake is a necessary consideration in energy balance, factors such as sex, age, and genotype, which have foiled the attempts of others to establish valid equations for prediction of body weight, may also be involved in this response. A strong hereditary component of body weight gives reason to believe that thin smokers will remain relatively thin as nonsmokers, and obese persons will remain obese regardless of their smoking habits. Leslie O. Schulz, Ph. D.
SUBJ K1, CESSATION
CD APRIL 2, 1987 JD/WC
UDT MAY 1, 1987 SHB

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REC 001379
AU Schulz,LO; Grunberg,NE; Jonas,S; Benowitz,NL; Hofstetter,A; Schutz,Y; Jequier,E; Wahren,J
TTL
CT Increased 24 Hour Energy Expenditure In Cigarette Smokers
Correspondence
DT
SUM The authors used one-tailed tests for all statistical analyses, under the assumption that smokers will have worse outcomes than reformed smokers. This seems appropriate on the basis of the literature. However, in a previous study, which served as the basis for the present one, the authors found smoking to be associated with improved survival after initial cardiac arrest. Hence, at worst the one-tailed test for significance should have been in this direction, or more reasonably, a two-tailed test should have been used. In any longitudinal study, bias can be introduced by nonuniform follow-up and expectations on the part of study personnel and subjects. The authors do not explicitly define how often and over what period outcome measures were evaluated. Was this a prospective study or a historical cohort study? Was the length of follow-up equal in each group? Recall bias also could have adversely influenced the findings. Questionnaires on smoking history were addressed not only to patients but also to family members if patients were unavailable. Family members' recall of the cause of death and smoking history of the patient could have been distorted if they were aware of the study questioning and proposed relation of smoking to the prognosis of patients with coronary artery disease.
SUBJ K1C, CESSATION, STATISTICS
CD APRIL 2, 1987 JD/WC
UDT MAY 1, 1987 SHB

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REC 001380
AU Schulz,LO; Grunberg,NE; Jonas,S; Benowitz,NL; Hofstetter,A; Schutz,Y; Jequier,E; Wahren,J
TTL
CT Increased 24 Hour Energy Expenditure In Cigarette Smokers
Correspondence
DT
SUM The authors used one-tailed tests for all statistical analyses, under the assumption that smokers will have worse outcomes than reformed smokers. This seems appropriate on the basis of the literature. However, in a previous study, which served as the basis for the present one, the authors found smoking to be associated with improved survival after initial cardiac arrest. Hence, at worst the one-tailed test for significance should have been in this direction, or more reasonably, a two-tailed test should have been used. In any longitudinal study, bias can be introduced by nonuniform follow-up and expectations on the part of study personnel and subjects. The authors do not explicitly define how often and over what period outcome measures were evaluated. Was this a prospective study or a historical cohort study? Was the length of follow-up equal in each group? Recall bias also could have adversely influenced the findings. Questionnaires on smoking history were addressed not only to patients but also to family members if patients were unavailable. Family members' recall of the cause of death and smoking history of the patient could have been distorted if they were aware of the study questioning and proposed relation of smoking to the prognosis of patients with coronary artery disease.
SUBJ V1, RESEARCH CRITICISM
CD APRIL 2, 1987 JD/WC
UDT MAY 1, 1987 SHB

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